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10/694,432	10/27/2003	Kathleen C.M. Campbell	SIU 7399	8934

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EXAMINER	
ROYDS, LESLIE A	
ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspatents@senniger.com

Office Action Summary	Application No.	Applicant(s)	
	10/694,432	CAMPBELL, KATHLEEN C.M.	
	Examiner	Art Unit	
	LESLIE A. ROYDS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-13,15-25,27-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-13,15-25,27-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *14May08 and 10June08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-9, 11-13, 15-25 and 27-33 are presented for examination.

A request for continued examination under 37 C.F.R. 1.114, including the fee set forth in 37 C.F.R. 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. 1.114, and the fee set forth in 37 C.F.R. 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 C.F.R. 1.114. Applicant's payment filed February 14, 2008 to enter the after-final submission dated December 20, 2007 has been received and entered into the present application. Accordingly, prosecution has been reopened.

Applicant's Information Disclosure Statements (IDS) filed May 14, 2008 (two pages) and June 10, 2008 (three pages) have each been received and entered into the present application. As reflected by the attached, completed copies of form PTO/SB/08(a) (five pages total), the Examiner has considered the cited references.

Claims 1-9, 11-13, 15-25 and 27-33 remain pending and under examination. Claims 30-33 are newly added.

Applicant's remarks, filed December 20, 2007, have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and objections are either reiterated or newly applied. They constitute the complete set of rejections and objections presently being applied to the instant application.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-3, 5-9 and 23-24 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant

regards as the invention, for the reasons of record set forth at p.2-3 of the previous Office Action dated September 14, 2007, of which said reasons are herein incorporated by reference.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that the word "exposed" is the passive voice and, therefore, encompasses all "temporal relationships" between administration of the methionine protective agent and the radiation exposure such that the scenarios defined in instant claims 2-3, 5-9 and 23-24 are not indefinite.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Applicant's argument is unpersuasive. The allegation that the term "exposed" is the passive voice is not a point well taken because the word "exposed" is simple past tense and clearly circumscribes a patient that has already been exposed to radiation for a time and at intensity sufficient to result in alopecia. In view of this fact, it is herein reiterated that the administration of the methionine protective agent prior to or simultaneously with radiation exposure in a patient who has already been exposed to radiation is an administration scenario that is impossible to execute. This is because it would be generally impossible to administer the methionine prior to or simultaneously with the radiation exposure if the patient has already been exposed to the radiation. Accordingly, the rejection remains proper despite Applicant's remarks to the contrary.

For these reasons *supra*, and those previously made of record at p.2-3 of the Office Action dated September 14, 2007, rejection of claims 2-3, 5-9 and 23-24 remains proper.

Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9, 11-13, 15-25 and 27-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pallenberg et al. (U.S. Patent No. 5,538,945; 1996) in view of Remington's Pharmaceutical Sciences (p.702-703; 1975).

Present claims 2-3, 5-9 and 23-24 are not included in the present rejection because they fail to further limit the subject matter of the parent claim from which they depend for the reasons described *supra* under 35 U.S.C. 112, second paragraph, and also because they are directed to an administration scenario that is not possible to execute (i.e., because it would be impossible to administer the protective agent prior to radiation exposure if the patient of the independent claim must have already been exposed to the radiation to induce the alopecia).

Pallenberg et al. teaches peptide-copper complexes and compositions containing the same for stimulating the growth of hair in warm-blooded animals, wherein the compositions include one or more peptide-copper complexes in combination with an acceptable carrier or diluent (col.1, l.65-col.2, l.4). Pallenberg et al. teaches that the peptide-copper complexes are administered to an animal in need thereof in a manner which results in the application of an effective amount of the peptide-copper complex, wherein the effective amount in an amount that stimulates hair growth, such as that caused by a hair-loss insult, i.e., radiation or chemotherapy (referred to in Pallenberg et al. as "secondary alopecia" as defined at col.7, l.6-10), wherein the complexes may be administered by, *inter alia*, injection (e.g., intramuscular, intravenous, subcutaneous or intradermal) (col.2, l.5-17). Pallenberg et al. teaches that the disclosed peptide-copper complexes have the structure [R1-R2]:copper(II), wherein R1 is an amino acid or derivative thereof and R2 is histidine, arginine, or a derivative thereof (col.2, l.22-32), wherein the amino acid may be, *inter alia*, methionine (M) (i.e., which meets Applicant's limitation that the methionine compound to be administered may be in the form of a salt as recited in instant claims 1, 22 and 30; col.3,

l.47-57). Pallenberg et al. teaches that the complexes may be used to treat hair loss secondary to chemotherapy and/or radiation treatment (i.e., understood to be a teaching that the complex may be administered *subsequent or after* radiation exposure) and also that the complex may be used to stimulate hair growth prior to an insult that would normally result in hair loss, such as chemotherapy or radiation regimens (i.e., understood to be a teaching that the complex may be administered *prior to* radiation exposure). Pallenberg et al. further teaches that the complexes encompass the use of both the naturally occurring L-form of the disclosed amino acid, as well as the D-form (col.7, l.46-52) and that the compositions of the complexes may be formulated in combination with carriers or diluents that provide for sustained release of the complex over time (col.8, l.35-40). Exemplary complexes according to the invention were studied in Example 15, wherein alopecia was induced via the chemotherapeutic agent cytosine arabinoside (Ara-C) and the exemplary peptide-copper complex was administered at a dosage of 50 mg/kg and resulted in body hair retention (col.24-25, Example 15).

Regarding Applicant's limitations directed to the administration of an effective amount that results in a blood serum level equivalent to that achieved by parenteral administration in the range of from 1.0-600 mg/kg body weight (claims 15 and 22) or 5-500 mg/kg body weight (claim 16) or 10-400 mg/kg body weight (claim 17), it is noted that, though Pallenberg et al. exemplifies the intraperitoneal injection of a specific peptide-copper complex at a dosage of 50 mg/kg (Example 15), the teachings and disclosure of the reference are not limited to that which is exemplified. In fact, Pallenberg et al. states at col.26, l.30-35, "From the foregoing, it will be appreciate that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention." Such a statement is clearly indicative of the fact that other complexes falling within the scope of the invention disclosed by Pallenberg et al. may be used in a substantially equivalent amount (i.e., parenteral injection of 50 mg/kg of the complex), even though they may not have been specifically exemplified. In fact, one of ordinary skill in the art would have

understood the exemplified dosage of the complex as guidance for using other complexes in a substantially equivalent amount with at least a reasonable expectation of successfully achieving a hair retaining effect. Furthermore, the fact that Pallenberg et al. disclosed a genus of peptide-copper complexes that are substantially interchangeable for achieving the disclosed hair-loss treating effect supports the determination that the use of other peptide-copper complexes within the scope of the disclosed genus would reasonably achieve this same hair-retaining effect in a patient with secondary alopecia in a substantially equivalent amount, absent factual evidence to the contrary.

Pallenberg et al. fails to teach (1) further administering a supplemental amount of the methionine agent after administration of the effective amount (claims 18 and 27), (2) wherein the administration of the supplemental amount is sufficient to maintain an effective blood serum level of the agent in the patient for a period of from 1-14 days after administration of the effective amount (claims 20 and 28), (3) wherein the administration of the supplemental amount is sufficient to maintain a blood serum level of at least 10% of the blood serum level achieved by administration of the effective amount (claims 21 and 29) and (4) administration of the methionine agent simultaneously with radiation exposure (claim 32).

One of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to administer a supplemental amount of the peptide-copper complex therapy of Pallenberg et al. for the purpose of treating secondary alopecia resulting from radiation exposure because the peptide-copper complexes were disclosed as having efficacy in ameliorating hair loss as it results from radiation regimens and, thus, the administration of a supplemental amount for the same purpose would have been reasonably expected to provide at least additive protective effects against hair loss resulting from radiation regimens as compared to a single administration of the same, absent factual evidence to the contrary. Such a person would have been motivated to do so (and, in particular, to provide an amount to the patient in need thereof sufficient to maintain an effective blood serum level of the agent for a period of from 1-14 days after administration of the first initial effective amount) in order to provide a baseline

plasma concentration of the active peptide-copper complex to provide hair-protecting effects throughout a treatment regimen of repeated sessions of radiation so as to maximize hair retention during a process (i.e., radiation) that normally results in hair loss. The determination of the optimum amount of time (i.e., from 1-14 days after administration of the first initial effective amount) over which to maintain an effective blood serum level of the agent would depend upon a variety of factors, including how many times the patient was exposed to radiation (i.e., number of radiation sessions over a period of time), the intensity of the radiation and the extent of hair loss as a result of the radiation. As a result, the amount sufficient to maintain an effective blood serum level for a period of from 1-14 days that would have actually been employed would have varied widely depending upon the radiotherapy regimen and, in the absence of evidence to the contrary, the currently claimed amount necessary to provide an effective amount for 1-14 days after administration of the first initial effective amount would not have been inconsistent with that which would have been determined by the skilled artisan, absent factual evidence to the contrary.

Remington's Pharmaceutical Sciences teaches that multiple dose administration may be used when the duration of therapy exceeds the effective sojourn of the drug in the body when used as a single administration (p.702). Remington's further teaches that, for multiple dose administrations, a dose is used wherein the plasma concentration rises to a maximum (Cmax) after each administration and falls to a minimum (Cmin) (p.702) such that the dosage interval effectively reaches a plateau wherein the absorption, distribution and elimination have reaches a fluctuating steady state concentration (p.702).

One of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to administer the supplemental dose of the complex in an amount sufficient to maintain a blood serum level of at least 10% of the blood serum level achieved by administration of the initial effective amount because the skilled artisan would have been motivated to administer a dosage effective to provide a rate of absorption, distribution and elimination that was essentially equivalent so as to result in a steady state plasma concentration during multiple dosing (i.e., the initial effective amount as disclosed by

Pallenberg et al. plus the subsequent supplemental amount). Such a person would have been motivated to do so in order to provide a plasma concentration of the active agent that is effective to achieve the claimed purpose of treating alopecia secondary to radiation while accounting for the body's natural rate of distribution and elimination of the active agent so as to maintain a steady state plasma concentration of the active agent, absent factual evidence to the contrary.

Lastly, one of ordinary skill in the art at the time of the invention would have also found it *prima facie* obvious to administer the active complex of Pallenberg et al. simultaneously with the patient's exposure to radiation because the complex is disclosed as having efficacy in treating alopecia secondary to radiation exposure and is also disclosed as being effective when administered parenterally (i.e., by various methods of injection), which is a route of administration that provides rapid distribution throughout the bloodstream as evidenced by Remington's Pharmaceutical Sciences (p.684), and, thus, the administration of the active complex via a parenteral route simultaneously with radiation exposure would have been reasonably expected to provide substantially equivalent efficacy to that obtained when the agent is administered prior to or after radiation exposure because the use of parenteral administration would have provided rapid distribution of the active complex throughout the bloodstream and allowed rapid onset of its hair-retaining effects. Such a person would have been motivated to do so because the rapid onset of efficacy using a parenteral route of administration of the active agent would have been indicative of the fact that the desirable therapeutic effect would have been provided immediately at the onset of radiation exposure and, therefore, would have reduced the amount of hair loss that would normally result from such radiation exposure, absent factual evidence to the contrary.

Conclusion

Rejection of claims 1-9, 11-13, 15-25 and 27-33 is proper.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LESLIE A. ROYDS whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

May 11, 2009